

BIOTERRORISM WATCH

Preparing for and responding to biological, chemical and nuclear disasters



Pathogens on a plane: The XDR-TB case in the age of bioterror

Those incubating disease are the real sleeper cells

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Questions regarding homeland security, bioterrorism, and containment of emerging infectious diseases have been raised in the aftermath of the recent, highly publicized case of the airline traveler with extensively drug-resistant tuberculosis (XDR-TB). The fact that the Atlanta man successfully eluded federal quarantine efforts and managed to cross the Canadian border despite orders to detain him has opened the federal agencies involved to criticism in congressional hearings.

"We dodged a bullet," said Rep. **Bennie Thompson** (D-MS), chairman of the Homeland Security Committee. Noting that the 9/11 Commission had found "a failure of imagination" among intelligence officials and Hurricane Katrina postmortems saw "a failure of initiative," Thompson said officials in this case "should have connected more dots." Officials testifying in the aftermath of the case outlined an array of failures that several members of Congress called "a wake-up call for a serious bioterrorism incident," according to press reports.¹

Counterterrorism planners such as **Jason D. Söderblom**, an analyst for the Terrorism Intelligence Centre in Canberra, Australia, have researched scenarios in which terrorists intentionally infect themselves with diseases including plague or smallpox and try to start an outbreak before succumbing to the illness. Indeed, Söderblom outlines a chilling "piggyback" scenario — using both smallpox and pneumonic plague — that has infected terrorists going to crowded clinics and waiting rooms in hospitals and physician offices while suffering from "flu-like" symptoms to mask their true disease and purpose.² (See related story, p. 20.)

He points out in a paper on the subject that biological warfare in the ancient world included use of "smallpox martyrs" and "poison maidens" as weapons against enemies. "Biological ruses using contaminated humans to counter strong military powers have an ancient and terrifying pedigree in both legend and fact," he wrote. ". . . Democracies, even in the broad definition of the term, are poorly organized to prevent a suicide bioterrorist from entering a public space, such as an airport, stadium, school, or shopping mall, and

spreading a biological weapon before the symptoms become apparent.”

Catch me if you can

But what of our more recent international incident, the elusive travels of the man with XDR-TB? While there appears to be considerable confusion about who said what to whom, the man was allegedly advised not to travel before doing so, setting off a one-man test of the international infectious disease warning and containment system in a series of plane rides and border crossings that played out like the sequel to *Catch Me If You Can*. Unfortunately, passengers on the flights in question became unwitting test subjects in a real-life clinical trial that asks the question: Can XDR-TB be transmitted from an apparently asymptomatic but potentially infectious patient to those seated nearby? The Centers for Disease Control and Prevention (CDC) notified all U.S. passengers on the international flights in question and advised

them to seek TB testing. Previous investigations indicate that air travel passengers with symptomatic TB (e.g., coughing) can transmit the disease during prolonged flights.^{3,4}

In this case, the answer will not be known for weeks and months as follow-up and testing continues through TB's potentially prolonged incubation period. However, it is doubtful transmission occurred in the absence of symptoms. Another encouraging finding is that none of the passenger's friends or family have been found to be infected. The man is undergoing treatment at the National Jewish Medical and Research Center in Denver. He originally was considered infectious based on three respiratory tract specimens that were reported culture positive for XDR-TB, the CDC reported. However, subsequent news reports had the hospital listing him as “relatively noncontagious,” based on sputum tests taken since his return to the states.

“While he may not have been highly infectious, he certainly was potentially capable of transmitting this infection to someone else,” **Julie Gerberding, MD**, CDC director, said at a recent press conference. “. . . We really had to be assertive as a public health agency in protecting people in this case because of the nature of the bacteria.” Indeed, the CDC had to pull out all the stops because XDR-TB is an absolutely unforgiving and virtually untreatable infection. By the current definition, XDR-TB is resistant to at least isoniazid and rifampin among the first-line anti-TB drugs and among second-line drugs is resistant to any fluoroquinolone and at least one of three injectable drugs. The staggering mortality rates among the HIV-infected in Africa are only part of the XDR-TB story. Unpublished CDC data indicate that the chances for survival — even in a person *without* HIV — are worse than 50/50 within four years of acquiring XDR-TB. A cancer diagnosis carries better odds — 55% survival rate within five years.

The follow-up and after-action analysis of this case at the CDC and among its international partners will be critical as XDR-TB continues to emerge globally, pandemic flu threatens to emerge, and the scenario of intentional infection continues to be discussed in bioterrorism circles. One obvious question is whether — had he been symptomatic — would the infected traveler been detected and barred from travel by public health, customs, and airport officials? “This is one case, but there are actually many, many cases where we have been successful,” Gerberding said. “Obviously this [case] has been very visible, but what's not visible

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Editorial Questions

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to you are the many patients [with] tuberculosis where health officials have been notified, patients have complied voluntarily with the recommendations and advice, and there has not been a risk to other people in the community.”

Gaps in the quarantine system

Still, in 2004, a man suffering from fever, chills, severe sore throat, and diarrhea flew from Sierra Leone to Newark, NJ. He died from Lassa fever less than a week after arrival, having exposed 188 people to the disease. That case was cited by the Institute of Medicine (IOM) in a 2005 report on the need for improving the current quarantine system.⁵ Indeed, the XDR-TB case actually may speed along ongoing improvements in the quarantine system and strengthen international partnerships, pushing ahead an effort that earlier was redoubled after the IOM report. Noting that some 120 million people travel into or out of the country through the nation’s 474 airports, seaports, and land-border crossings every year, the IOM warned that the system of using CDC quarantine stations no longer is sufficient to protect the population against microbial threats of public health significance that originate abroad. The current list of federally authorized quarantinable communicable diseases includes cholera, diphtheria, infectious tuberculosis, plague, smallpox, yellow fever, viral hemorrhagic fevers (Lassa, Marburg, Ebola, etc.), severe acute respiratory syndrome (SARS), and flu strains that have the potential to cause a pandemic.

One significant gap in the current quarantine system is the difficulty involved in quickly locating airline passengers who may have been exposed to a high-risk infectious agent such as the SARS virus during a flight, the IOM reported. Often, travelers have to be found days after the flight is over. The IOM report supported the targeted use of passenger locator cards as an interim solution. The cards — which would be distributed on flights to and from countries where a disease outbreak is occurring or when a passenger or crew member becomes ill during a flight — would record passenger contact information and seat numbers in a scannable format so that the data could be retrieved and transmitted easily. In addition, in a conclusion that seems prescient regarding the XDR-TB fiasco, which involved travel of an asymptomatic passenger, the IOM report concludes: “infected individuals and animals do not necessarily develop signs of disease while in transit or by the time of arrival, and available noninvasive diagnostics cannot always identify

infected travelers with reasonable sensitivity, specificity, and speed.”

Indeed, much of the hue and cry over the XDR-TB case has overshadowed a more insidious reality in daily global air travel: A passenger in the incubation stages of some emerging infectious disease could be headed to any given U.S. community and there is very little that anyone can do about it. Such infected passengers may be traveling from one of the 17 countries that have reported XDR-TB. Air travel connecting any two points in the world can certainly be accomplished well within the prolonged incubation period for TB and for the vast majority of other infectious diseases as well. The 2003 emergence of SARS in Hong Kong was fueled by rapid global spread via air travel. While airline passengers were at risk of SARS transmission, the real outbreak occurred in various nations after those incubating and infected had deplaned. In that regard, much of the coverage and discussion of the XDR-TB case has missed the point, says **Eric Toner, MD**, senior associate at the Center for Biosecurity at the University of Pittsburgh Medical Center. While a passenger infecting others on a plane would be a public health incident, the asymptomatic passenger whose infection will appear later is the real threat of a major biological event, he notes.

“The issue with infectious diseases and travel is not that someone contagious would get on an airplane, but rather that people who are incubating can travel around the world, as happened with SARS,” he says. “For the most part, they didn’t transmit the disease on the airplane but within the country they were traveling to once they got there. And there is no way through regulations and technology to identify people with incubating disease. That’s the real issue.”

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Bioterror scheme: Infected terrorists in waiting room

A one-two punch using smallpox and plague

A counterterrorism researcher has conjured up a dark thought problem for other planners in emergency response and medical care to ponder. What if intentionally infected terrorists — some with smallpox, others with pneumonic (e.g., airborne) plague — coordinated an attack that used medical settings as one of its prime sites of initial exposures?

“The suicide ‘martyr’ scenario posed in this report is logically feasible . . .” concludes a counterterrorism expert at the Terrorism Intelligence Centre in Canberra, Australia.¹ “Improvements can, however, be made; they will ultimately include research into rapid confirmation tests for the plague and smallpox, the development of antiviral drugs, biochemical awareness training for all physicians and hospital staff, and anti-terrorist initiatives aimed at preventing ‘conversions’ to militant organizations.”

Here is summary of the key points in the scenario:

- **Smallpox component:** Smallpox — which most of the U.S. population is susceptible to — spreads directly from person to person, primarily by droplet nuclei expelled from the oropharynx (the space beneath the mouth cavity) of the infected person or can be disseminated by aerosol spray. Natural infection occurs following implantation of the virus on the oropharyngeal or respiratory mucosa. Exposure to smallpox could, therefore, occur through inhalation of an aerosol or exposure to droplets through a “suicide carrier.” Intelligence agencies and international relations scholars are concerned that Russian researchers of the former Biopreparat, many whom have been unemployed since the 1990s and feel disenfranchised, could be tempted to smuggle and sell smallpox to those terrorist groups with the financial resources and microbiological expertise to use it, or further weaponize it.

- **Pneumonic plague component:** A suicide terrorist infected with the pneumonic plague would not look out of place in a hospital ward or a physician’s [office], while he or she spread the plague. The suicide pneumonic plague carrier would not be seeking to be diagnosed with the plague but would be relying on the “flu-like symptoms” to remain undiagnosed. The terrorist

may also stay long enough to spread the plague, but leave before the physician examines him or her. It is often assumed that the “visible sickness” of the plague-infected terrorist would make plague-based bioterrorism easily detected, but spreading the pneumonic plague at hospitals makes its symptoms less suspicious than coughing heavily on trains, in the workplace or in foyers of Congress or Parliament. Not only is plague highly fatal and contagious, it also is stored in microbe banks around the world. In the 1950s and 1960s, there were many institutions and thousands of scientists studying variants of the plague. It thus remains probable that this expertise could be purchased at any time.

- **Suicide Martyr Scenario:** In this scenario, two “suicide pneumonic plague-infected terrorists” strategically target doctors’ offices (in winter) to obtain a medical certificate to explain their absence from work. (They could even leave before seeing the physician.) They blend in with people suffering flu symptoms in the waiting room, but they are already effectively spreading the pneumonic plague amongst staff and patients. A terrorist organization claims responsibility for the plague outbreak. Citizens are too terrified to seek medical attention, as they now are aware that medical facilities have been targeted. This is when the second stage of the bioterror attack occurs. Smallpox is delivered to the target city through either aerosolized delivery, or through an infected set of suicide terrorists passing on smallpox through exhaled droplets.

Mass terror is created by the paradox that smallpox needs to be contained and treated, yet the mass plague (and smallpox) infection of patients and staff at hospitals causes citizens to stay away from medical facilities. A radio talk-back host ponders on-air whether by attending the doctor to get checked for the flu, or vaccinated for smallpox, you may acquire both the pneumonic plague and smallpox before the vaccination takes effect. Large segments of the community avoid medical treatment. The strain placed on the infrastructure of the city brings it to a halt: Planes do not arrive or leave, police at roadblocks turn back fleeing residents, and the “terror” caused by the bioterror attack is unmatched by any previously experienced health catastrophe. The economy is brought to a standstill and the bioterrorists now have political influence as they have demonstrated their capacity to inflict terror. Worse still, a rumor circulates that the smallpox is a weaponized variant from the former USSR, for which there is no vaccine. Thus, the containment of infected people proves to be impossible even

though the World Health Organization vaccines arrive quickly. There are not enough respirator masks to go around.

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Train wrecks prompt chemical terror warning

Hospitals in any area could face surge of pts

A series of hazardous substance spills and accidents on the nation's rail system has prompted the Centers for Disease Control and Prevention (CDC) to warn "of the potential for terrorist attacks on railcars carrying large quantities of hazardous substances."¹ Though terrorism is not suspected in the incidents, the accidents reveal existing vulnerabilities as well as the potential for major community disruption and potential mass casualties.

To meet the threat and prevent unintentional chemical releases, the CDC called for increased collaboration among railroad stakeholder organizations (e.g., environmental, transportation, industry, public health, public safety, and research) to develop better mechanisms to monitor rail substance-release events and use available data to identify vulnerabilities and promote safer technologies and practices. "Additional preparedness measures (e.g., planning and training of local response agencies and the public and establishment of notification mechanisms, escape routes, shelter-in-place protocols, and emergency shelters) are needed to respond to hazardous-substance rail incidents," the CDC noted. Hospitals located in communities where such chemicals are regularly railed through should be aware that they could face a rapid surge of patients following an accident and release of a chemical such as chlorine.

"The biggest problem that hospitals have in responding to chlorine or a similar respiratory irritant chemical agent is the huge number of people who have potentially serious injury to their lungs all arriving in a relatively short period of time," says **Eric Toner**, MD, senior associate at the Center for Biosecurity at the University of Pittsburgh Medical Center. "One of the areas where we really have

limited surge capacity is the area of mechanical ventilators. It would be very hard to mobilize enough ventilators in a very short period of time if we have huge numbers of people exposed to very toxic levels of these respiratory agents."

Residual chemical agents on those exposed may pose a risk of secondary spread to workers, as evidenced by pesticide patients presenting at emergency departments. Three health care workers — one who was subsequently hospitalized for nine days — fell ill after a patient who had ingested pesticide came into an emergency department in a South Georgia hospital in 2000. As a result of the case, the CDC recommended staff take personal protection measures beyond standard infection control precautions.² Depending on the extent of the contamination, health care workers caring for chemically contaminated patients should use Level C protection (i.e., full face mask and powered/nonpowered canister/cartridge filtration respirator) or Level B protection (i.e., supplied air respirator or self-contained breathing apparatus). The type of canister/cartridge should be appropriate to the agent. If the agent cannot be identified, use an organic vapor/HEPA filter, the CDC recommended.

South Carolina disaster kills nine

Although the rate of all rail incidents has declined sharply since 1980, less improvement has been observed in recent years; the rail incident rate per million train miles actually increased from 3.76 in 2002 to 4.38 in 2004, before decreasing to 4.08 in 2005, the CDC reported. In recent years, concern over railroad safety has been elevated by major incidents such as the Graniteville, SC, train collision in January 2005 that released 11,500 gallons of chlorine gas, caused nine deaths, and resulted in 529 people seeking medical treatment, the CDC noted. In response, the U.S. Department of Transportation (DOT) and the Federal Railroad Administration launched the National Rail Safety Action Plan in 2005. The plan targets the most frequent, highest-risk causes of train incidents (e.g., equipment failure or human error) and is aimed at improving emergency preparedness and the safe handling of hazardous materials. In addition, in 2006, the DOT proposed new rules requiring rail carriers to compile annual data on hazardous materials shipments and use those data to evaluate safety and security risks and alternative routing options, the CDC reported.

Another incident occurred this year, however,

underscoring that even less severe accidents can cause major disruption. On Jan. 16, a train with 12 carloads of hazardous materials or residue derailed in Brooks, KY. Tank cars containing 1,3-butadiene, cyclohexane, methyl ethyl ketone, and maleic anhydride were allowed to burn throughout the night to destroy the hazardous materials. These chemicals were detected in air and water samples from the area surrounding the incident site. Thirty-one area residents immediately reported symptoms that included headache, dizziness, upper and lower respiratory tract irritation, and eye irritation. A total of 53 people in the vicinity eventually sought medical treatment at two local hospitals, including a woman who needed two weeks of supportive therapy. In addition, 35 residents of 15 homes were prohibited from returning home for approximately six weeks until contaminated plastic water lines (penetrable by released chemicals) were

replaced. Approximately 300 people from outside the evacuation area but within the path of the plume were ordered to shelter in place.

Iraq attacks use chlorine as weapon

Terrorists conducted a chemical attack on civilians in Tokyo in 1995, when 12 people were killed and 5,000 injured in the attack by the Aum Shinrykyo cult. Counterterrorism planners looking back at that attack note that it could have been considerably more deadly had the terrorists come up with a better delivery system. The inclination to use chemical materials as weapons recently has been underscored by insurgent attacks in Iraq involving chlorine-containing trucks.

“We have known since 9/11 of the threat of both weaponized chemical agents and also commercial chemical agents and the threat they pose in the

Quick facts about chlorine: From WWI to the local pool

No antidote exists for chlorine exposure

The Centers for Disease Control and Prevention (CDC) provides a few quick facts about chlorine, one of the more dangerous chemicals regularly transported throughout the nation.

- Chlorine is an element used in industry and found in some household products.

- It is sometimes in the form of a poisonous gas.

The gas can be pressurized and cooled to change it into a liquid so that it can be shipped and stored. When liquid chlorine is released, it quickly turns into a gas that stays close to the ground and spreads rapidly.

- Chlorine gas can be recognized by its pungent, irritating odor, which is like that bleach. The strong smell may provide an adequate warning to people that they have been exposed. The gas appears to be yellow-green in color.

- It is not flammable, but it can react explosively or form explosive compounds with other chemicals such as turpentine and ammonia.

- It was used during World War I as a choking (pulmonary) agent.

- It is one of the most commonly manufactured chemicals in the United States. Its most important use is as a bleach in the manufacture of paper and cloth, but it also is used to make pesticides (insect killers), rubber, and solvents.

- It is used in drinking water and swimming pool water to kill harmful bacteria. It also is used as part of the sanitation process for industrial waste

and sewage.

- Household chlorine bleach can release a gas if it is mixed with other cleaning agents.

- The extent of poisoning depends on the amount a person is exposed, how the person was exposed, and the length of time of the exposure.

- When chlorine gas comes into contact with moist tissues such as the eyes, throat, and lungs, an acid is produced that can damage these tissues.

- **Signs and symptoms of exposure:** During or immediately after exposure to dangerous concentrations of chlorine, the following signs and symptoms may develop:

- coughing;

- chest tightness;

- burning sensation in the nose, throat, and eyes;

- watery eyes;

- blurred vision;

- nausea and vomiting;

- burning pain, redness, and blisters on the skin if exposed to gas, skin injury similar to frostbite if exposed to liquid;

- difficulty breathing or shortness of breath (may appear immediately if high concentrations of chlorine gas are inhaled, or may be delayed if low concentrations of gas are inhaled);

- fluid in the lungs (pulmonary edema) within two to four hours.

- Those exposed should remove clothing, rapidly wash entire body with soap and water, and get medical care as quickly as possible.

- No antidote exists for chlorine exposure. Treatment consists of removing the chemical from the body as soon as possible and providing supportive medical care in a hospital setting. ■

hands of terrorists," Toner says. "It's actually surprising to me that the insurgents in Iraq had not done this previously. But I don't think it changes anything fundamentally for us. It's a big threat and one that has not been addressed adequately. We still see trains with toxic substances going through the middle of cities and tanker trucks on the highway. The hard question is, 'How are going to get the material where it needs to go?' There is no easy answer for that. Our economy and industry depend on these chemicals. They are essential parts of many manufacturing processes."

Every year, nearly 2 million train carloads of hazardous substances move along the rails throughout the nation, rolling into many densely populated areas in the process. Notably, about 81% of hazardous substance releases from rail events occurred in areas with residences within a quarter-mile and most of the injured were members of the general public. Of these aforementioned carloads, more than 100,000 will contain toxic inhalation hazard substances such as chlorine, anhydrous ammonia, and hydrochloric acid. Although rail events constitute only 2% of total hazardous substance releases, such incidents can cause severe public health consequences, the CDC emphasized. The scenarios ratchet up considerably when a terrorist attack is included. Consider a few cogent points drawn from a paper published last year by **Lawrence M. Wein**, PhD, the Paul E. Holden Professor of Management Science at Stanford University³:

- A terrorist attack on a single 90-ton chlorine tank car could generate a cloud of toxic gas that travels 20 miles. If the attack took place in a city, it could kill 100,000 people within hours. Now multiply that nightmare by another 100,000. That's the approximate number of tank cars filled with toxic gases shipped every year in the United States.

- The most dangerous chemicals are those that, on release, form heavier-than-air clouds that can travel 10 to 20 miles. The three main culprits are chlorine (used in the production of building materials), anhydrous ammonia (used for agricultural fertilizer) and, worst of all, hydrofluoric acid (used in transportation fuels).

- Chlorine and anhydrous ammonia are not

CE/CME questions

- The case of the traveler with extensively drug-resistant tuberculosis (XDR-TB) raised discussion of infected terrorists intentionally exposing a population to disease. What was the historical term used to describe such infected terrorists?
 - smallpox martyrs
 - plague guests
 - poison maidens
 - A and C
- Previous investigations indicate that air travel passengers with symptomatic TB can transmit the disease during prolonged flights if they:
 - are seated near air recirculation intake.
 - have a cough or other symptoms.
 - constantly talk to nearby passengers.
 - have the XDR strain.
- Hospitals located in communities where railroads carry hazardous chemicals such as chlorine could face a rapid surge of patients with respiratory problems following an accident or attack. What item was cited as likely to be in short supply in such a scenario?
 - gloves
 - vaccine
 - mechanical ventilators
 - asthma medicines
- Fortunately, an antidote for chlorine exposure has long been available to quickly reduce patient symptoms.
 - True
 - False

Answer Key: 9. D; 10. B; 11. C; 12. B.

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stored in the vast quantities that hydrofluoric acid is at oil refineries, and the biggest threat from these chemicals may be during their transport in tank cars. To prevent these well-marked tank cars from injuring or killing tens of thousands of people, hazardous shipments must be routed away from densely populated areas.

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New biodefense panel formed to advise HHS

The Department of Health and Human Services (HHS) is establishing a public health advisory panel concerned with chemical, biological, nuclear, or radiological agents. The National Biodefense Science Board will give the HHS guidance on preventing, preparing for, and responding to release of such agents, whether they are naturally occurring, accidental, or deliberate.

The board, which was authorized by the Pandemic and All-Hazards Preparedness Act, will advise HHS Secretary **Mike Leavitt** about trends, challenges, and opportunities in the field. At the secretary's request, it also will provide recommendations for research and development. "This new advisory board will add a wide range of expertise and viewpoints from outside of government to help inform HHS decision-making processes," he said.

Board members are yet to be selected. There will be 13 members, appointed by the secretary, from among leading experts in science, public health, and medicine. The secretary also will appoint federal officials to support the board's functions.

To submit a resume or curriculum vitae for consideration to be a board member, e-mail nbsb_nominations@hhs.gov. For further information, contact Dr. Susan Cibulsky at (202) 260-7000 or e-mail nbsbquestions@hhs.gov. The board's charter and additional information can be found on-line at www.hhs.gov/aspr/omsph/nbsb. ■

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After reading each issue of *Bioterrorism Watch*, the infection control professional will be able to do the following:

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- describe how the issue affects health care providers, hospitals, or the health care industry in general;
- cite solutions to the problems associated with bioterrorism, based on guidelines from the federal Centers for Disease Control and Prevention or other authorities, and/or based on independent recommendations from clinicians and bioterrorism experts. ■

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